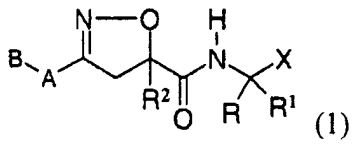
AMENDED SET OF CLAIMS

Please amend the claims as follows:

1. (Original) A compound of the following formula (1):



(1)

in which

I) R represents H, simple alkyl chain (-SAC), simple cycloalkyl chain (-SCAC), aryl group (-Ar), or simple alkyl chain substituted by aryl (-SAC-Ar),

II) R^1 represents -SAC, -SCAC, -Ar, -SAC-Ar, or a side chain residue of all the natural amino acids; and the compound of formula (1) may exist in a specific diastereomeric form, or mixtures thereof when the carbon to which R^1 is attached becomes a stereocenter due to the R^1 group; or the compound of formula (1) may have a protecting group in an ester form ($-CO_2R^3$ wherein R^3 is -SAC) or a sulfonamide form ($-CONHSO_2R^4$ wherein R^4 is -SAC), or may exist in the form of pharmaceutically acceptable salt, when R^1 is a side chain residue of an amino acid containing carboxyl moiety; or the compound of formula (1) may also exist in the form of pharmaceutically acceptable salt when R^1 is a side chain residue of an amino acid containing a base moiety,

III) R^2 represents -SAC, -SCAC, -Ar, -SAC-Ar, or a side chain residue of the natural amino acids; and the compound of formula (1) may exist in a specific

diastereomeric form, or mixtures thereof when the carbon to which R^2 is attached becomes a stereocenter due to the R^2 group; the compound of formula (1) may have a protecting group in an ester form ($-CO_2R^5$ wherein R^5 is -SAC) or a sulfonamide form ($-CONHSO_2R^6$ wherein R^6 is -SAC), or may exist in the form of pharmaceutically acceptable salt, when R^2 is a side chain residue of an amino acid containing carboxyl moiety; or the compound of formula (1) may also exist in the form of pharmaceutically acceptable salt when R^2 is a side chain residue of an amino acid containing a base moiety, or

R^2 further represents H; $-(CH_2)_nOR^7$ wherein R^7 is -SAC, -SCAC, -Ar, or -SAC-Ar, and n = 1 or 2; or $-(CH_2)_nOC(=O)R^8$ wherein R^8 is -SAC, -SCAC, -Ar, or -SAC-Ar, and n = 1 or 2,

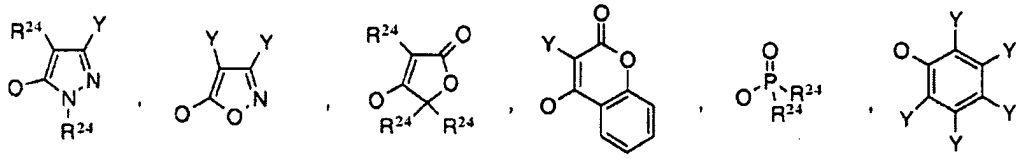
IV) A represents $-(CH_2)_n-$ (n = 0-4), $-O-(CH_2)_n-$ (n = 0-4), or $-NR^9-(CH_2)_n-$ (n = 0-4) wherein R^9 is -SAC, -SCAC, -Ar, or -SAC-Ar,

V) B represents H, -SAC, -SCAC, -Ar, or -SAC-Ar, or

VI) R and R^1 may form a cycle together with the carbon atom to which they are attached, where $-R-R^1-$ is $-(CH_2)_n-$, $-(CH_2)_n-O-(CH_2)_m-$, or $-(CH_2)_n-NR^{10}-(CH_2)_m-$ wherein n+m<9 and R^{10} is -SAC, -SCAC, -Ar, -SAC-Ar, -C(=O)-SAC, -C(=O)-SCAC, -C(=O)-Ar, or -C(=O)-SAC-Ar,

VII) X represents $-C(=O)CH_2OR^{11}$ wherein R^{11} is -SAC, -SCAC, -Ar, or -SAC-Ar; $-C(=O)CH_2OC(=O)R^{12}$ wherein R^{12} is -SAC, -SCAC, -Ar, or -SAC-Ar; $-CH=CH-CO_2R^{13}$ wherein R^{13} is -SAC, -SCAC, -Ar, or -SAC-Ar; -CH=CH-

SO_2R^{14} wherein R^{14} is -SAC, -SCAC, -Ar, or -SAC-Ar; $-C(=O)CH=CH_2$; or $-COCH_2$-W wherein W is $-N_2$, -F, -Cl, -Br, -I, $-NR^{15}R^{16}$ (R^{15} and R^{16} each are -SAC, -SCAC, -Ar, or -SAC-Ar, or together may form 3- to 6-membered saturated or unsaturated cyclic group), $-SR^{17}$ (R^{17} is -SAC, -SCAC, -Ar, or -SAC-Ar), or is the following formula:



wherein

Y is H, -OH, $-OR^{18}$ (R^{18} = -SAC or –SCAC), $-C(=O)R^{19}$ (R^{19} = -H, -SAC, or -SCAC), -F, -Cl, -Br, -I, -CN, -NC, $-N_3$, $-CO_2H$, CF_3, $-CO_2R^{20}$ (R^{20} = -SAC or -SCAC), $-C(=O)NHR^{21}$ (R^{21} = -SAC or -SCAC), or $-C(=O)NR^{22}R^{23}$ (R^{22} and R^{23} each are -SAC, -SCAC, -Ar, or -SAC-Ar),

R^{24} is H, -SAC, -SAC-Ar, or –Ar, salt, or stereoisomer thereof.

2. (Original) The compound according to claim 1 wherein R represents H.

3. (Original) The compound according to claim 1 wherein R^1 represents $-CH_2COOH$, $-CH_2COOR^3$ (R^3=SAC), or $-CH_2CONHSO_2R^4$ (R^4 = SAC).

4. (Original) The compound according to claim 1 wherein R^2 represents H, -SAC, -Ar, or $-(CH_2)_nOR^7$ (R^7 = -SAC, -SCAC, -Ar, or -SAC-Ar, and n = 1 or 2).

5. (Original) The compound according to claim 1 wherein X represents -C(=O)CH_2OAr, -C(=O)CH_2OC(=O)Ar, or -$COCH_2$-W wherein W is -N_2, -F, -Cl, -Br, -I, -$NR^{15}R^{16}$ (R^{15} and R^{16} each are -SAC, -SCAC, -Ar, or -SAC-Ar, or together may form 3- to 6-membered saturated or unsaturated cyclic group), or -SR^{17} (R^{17} is -SAC, -SCAC, -Ar, or -SAC-Ar).

6. (Original) The compound according to claim 1 wherein

I) R represents H,

II) R^1 represents -CH_2COOH, -CH_2COOR^3 (R^3=SAC), or -$CH_2CONHSO_2R^4$ (R^4 = SAC),

III) R^2 represents H, -SAC, -Ar, or -$(CH_2)_nOR^7$ (R^7 = -SAC, -SCAC, -Ar, or -SAC-Ar, and n = 1 or 2),

IV) A represents -$(CH_2)_n$- (n = 0-4) or -O-$(CH_2)_n$- (n = 0-4),

V) B represents H, -SAC, -SCAC, -Ar, or -SAC-Ar,

VI) X represents -$COCH_2N_2$, -$COCH_2F$, -$COCH_2Cl$, -$COCH_2Br$, -$COCH_2I$, -$COCH_2OAr$, -$COCH_2OCOAr$ or -$COCH_2SR^{17}$ (R^{17} is -SAC, -SCAC, -Ar or -SAC-Ar).

7. (Original) The compound according to claim 1 which is selected from the following group:

(1) (3*S*)-5-[(2,6-dichlorobenzoyl)oxy]-3-({[5-methyl-3-phenyl-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxopentanoic acid (Iaa);

(2) (3*S*)-3-({[5-methyl-3-phenyl-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxo-5-phenoxypentanoic acid (Ibb);

(3) (3*S*)-3-({[5-ethyl-3-phenyl-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)pentanoic acid (Icc);

(4) (3*S*)-3-({[5-ethyl-3-(1-naphthyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)pentanoic acid (Idd);

(5) (3*S*)-3-({[5-ethyl-3-(2-naphthyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)pentanoic acid (Iee);

(6) (3*S*)-3-({[5-ethyl-3-(1-isoquinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)pentanoic acid (Iff);

(7) 3-({[5-ethyl-3-(1-isoquinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-5-fluoro-4-oxopentanoic acid (Igg);

(8) ethyl 3-({[5-ethyl-3-(1-isoquinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-5-fluoro-4-oxopentanoate (Ihh);

(9) 5-fluoro-3-({[(5*R*)-5-isopropyl-3-(1-isoquinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxopentanoic acid (Iii);

(10) 3-({[5-ethyl-3-(4-quinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-5-fluoro-4-oxopentanoic acid (Ijj);

(11) 3-({[3-(benzothiophen-2-yl)-5-ethyl-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-5-fluoro-4-oxopentanoic acid (Ikk);

(12) (3S)-3-({[3-(1,3-dimethyl-1*H*-indol-2-yl)-5-ethyl-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)pentanoic acid (Ill);

(13) 3-({[3-(1,3-dimethyl-1*H*-indol-2-yl)-5-ethyl-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-5-fluoro-4-oxopentanoic acid (Imm);

(14) (3*S*)-3-({[5-ethyl-3-(1-naphthylmethyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)pentanoic acid (Inn);

(15) (3*S*)-5-[(2,6-dichlorobenzoyl)oxy]-3-[({5-ethyl-3-[2-(1-naphthyl)ethyl]-4,5-dihydro-5-isoxazolyl}carbonyl)amino]-4-oxopentanoic acid (Ioo);

(16) (3*S*)-3-[({5-ethyl-3-[(1-naphthyloxy)methyl]-4,5-dihydro-5-isoxazolyl}carbonyl)amino]-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)pentanoic acid (Ipp);

(17) (3*S*)-3-{[(3-{[(4-chloro-1-naphthyl)oxy]methyl}-5-ethyl-4,5-dihydro-5-isoxazolyl)carbonyl]amino}-4-oxo-5-(2,3,5,6-tetrafluorophenoxy)pentanoic acid (Iqq);

(18) (3*S*,4*E*)-6-ethoxy-3-({[(5*R*)-5-isopropyl-3-(1-isoquinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-6-oxo-4-hexenoic acid (Irr);

(19) (3*S*,4*E*)-3-({[(5*R*)-5-isopropyl-3-(1-isoquinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-5-(methylsulfonyl)-4-pentenoic acid (Iss);

(20) 5-fluoro-3-({[(5*S*)-3-(1-isoquinolinyl)-5-propyl-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxopentanoic acid (Itt);

(21) 3-({[(5*S*)-5-ethyl-3-(1-naphthyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-5-fluoro-4-oxopentanoic acid (Iuu);

(22) 3-({[(5*S*)-5-ethyl-3-(2-quinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-5-fluoro-4-oxopentanoic acid (Ivv);

(23) 3-({[(5*R*)-5-ethyl-3-(3-isoquinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-5-fluoro-4-oxopentanoic acid (Iww);

(24) 3-({[5-ethyl-3-(8-quinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-5-fluoro-4-oxopentanoic acid (Ixx);

(25) 3-({[5-ethyl-3-(3-quinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-5-fluoro-4-oxopentanoic acid (Iyy);

(26) 5-fluoro-3-({[(5*R*)-5-isopropyl-3-(2-quinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxopentanoic acid (Izz);

(27) 3-({[5-ethyl-3-(2-isopropylphenyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-5-fluoro-4-oxopentanoic acid (Iaa1);

(28) 3-[({3-[3-(*tert*-butyl)phenyl]-5-ethyll-4,5-dihydro-5-isoxazolyl}carbonyl)amino]-5-fluoro-4-oxopentanoic acid (Iaa2);

(29) 3-[({3-[4-(*tert*-butyl)phenyl]-5-ethyl-4,5-dihydro-5-isoxazolyl}carbonyl)amino]-5-fluoro-4-oxopentanoic acid (Iaa3);

(30) 5-fluoro-3-({[(5*R*)-5-isopropyl-3-(2-isopropylphenyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxopentanoic acid (Iaa4);

(31) 3-[({(5*R*)-3-[3-(*tert*-butyl)phenyl]-5-isopropyl-4,5-dihydro-5-isoxazolyl}carbonyl)amino]-5-fluoro-4-oxopentanoic acid (Iaa5);

(32) 3-{[(3-[1,1'-biphenyl]-3-yl-5-isopropyl-4,5-dihydro-5-isoxazolyl)carbonyl]amino}-5-fluoro-4-oxopentanoic acid (Iaa6);

(33) 3-({[5-ethyl-3-(2-pyridinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-5-fluoro-4-oxopentanoic acid (Iaa7);

(34) 3-[({3-[4-(*tert*-butyl)-2-pyridinyl]-5-ethyl-4,5-dihydro-5-isoxazolyl}carbonyl)amino]-5-fluoro-4-oxopentanoic acid (Iaa8);

(35) 3-[({(5*R*)-3-[4-(*tert*-butyl)-2-pyridinyl]-5-isopropyl-4,5-dihydro-5-isoxazolyl}carbonyl)amino]-5-fluoro-4-oxopentanoic acid (Iaa9);

(36) 3-({[5-ethyl-3-(4-isobutyl-2-pyridinyl)-4,5-dihydro -5-isoxazolyl]carbonyl}amino)-5-fluoro-4-oxopentanoic acid (Iaa10);

(37) 3-({[3-(4-acetyl-2-pyridinyl)-5-ethyl-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-5-fluoro-4-oxopentanoic acid (Iaa11);

(38) 3-({[3-(4-cyclopropyl-2-pyridinyl)-5-ethyl-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-5-fluoro-4-oxopentanoic acid (Iaa12);

(39) 3-({[3-(4-cyclopentyl-2-pyridinyl)-5-ethyl-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-5-fluoro-4-oxopentanoic acid (Iaa13);

(40) 3-({[(5*R*)-3-(4-cyclopentyl-2-pyridinyl)-5-isopropyl-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-5-fluoro-4-oxopentanoic acid (Iaa14);

(41) 3-({[3-(4-cyclohexyl-2-pyridinyl)-5-ethyl-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-5-fluoro-4-oxopentanoic acid (Iaa15);

(42) 3-({[5-ethyl-3-(5,6,7,8-tetrahydro-1-isoquinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-5-fluoro-4-oxopentanoic acid (Iaa16);

(43) 5-fluoro-3-({[5-isopropyl-3-(4-phenyl-2-pyridinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxopentanoic acid (Iaa17);

(44) (3*S*)-5-[(diphenylphosphoryl)oxy]-3-({[(5*R*)-5-isopropyl-3-(1-isoquinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxopentanoic acid (Iaa18);

(45) (3*S*)-3-({[(5*R*)-5-isopropyl-3-(1-isoquinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxo-5-{[1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl]oxy}pentanoic acid (Iaa19);

(46) (3*S*)-5-[(4-benzyl-5-oxo-2,5-dihydro-3-furanyl)oxy-3-({[(5*R*)-5-isopropyl-3-(1-isoquinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxopentanoic acid (Iaa20);

(47) (3*S*)-5-(isobutyryloxy)-3-({[(5*R*)-5-isopropyl-3-(1-isoquinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxopentanoic acid (Iaa21);

(48) (3*S*)-3-({[(5*R*)-5-isopropyl-3-(1-isoquinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxo-5-hexenoic acid (Iaa22);

(49) (3*S*)-3-({[(5*R*)-5-isopropyl-3-(1-isoquinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxo-5-(2-pyridinyloxy)pentanoic acid (Iaa23);

(50) (3*S*)-3-({[5-ethyl-3-(2-isopropylphenyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxo-5-(2-pyridinyloxy)pentanoic acid (Iaa24);

(51) 2-{[(3*S*)-4-carboxy-3-({[(5*R*)-5-isopropyl-3-(1-isoquinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-2-oxobutyl]oxy}-1-methylpyridinium trifluoromethanesulfonate (Iaa25);

(52) 2-{[(3*S*)-4-carboxy-3-({[5-ethyl-3-(2-isopropylphenyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-2-oxobutyl]oxy}-1-methylpyridinium trifluoromethanesulfonate (Iaa26);

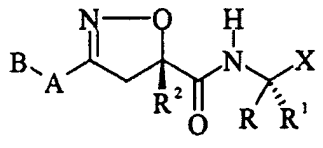
(53) 3-({[3-(5-chloro-1-methyl-1*H*-indol-2-yl)-5-isopropyl-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-5-fluoro-4-oxopentanoic acid (Iaa27);

(54) 3-({[3-(1,5-dimethyl-1*H*-indol-2-yl)-5-isopropyl-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-5-fluoro-4-oxopentanoic acid (Iaa28); and

(55) (3*S*)-5-fluoro-3-({[(5*R*)-5-isopropyl-3-(1-isoquinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxopentanoic acid (Iii-1).

8. (Original) The compound according to claim 1 which is 5-fluoro-3-({[(5*R*)-5-isopropyl-3-(1-isoquinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxopentanoic acid (Iii).

9. (Original) A compound of the following formula (1a):



(1a)

in which

A, B, R, R^1, R^2, and X are defined as described in claim 1.

10. (Original) The compound according to claim 9 which is (3*S*)-5-fluoro-3-({[(5*R*)-5-isopropyl-3-(1-isoquinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxopentanoic acid (Iii-1).

11. (Original) A process for preparing the compound (Iii-1) as defined in claim 10, which comprises the steps of dissolving a mixture of (3*S*)-5-fluoro-3-({[(5*R*)-5-isopropyl-3-(1-isoquinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxopentanoic acid and (3*R*)-5-fluoro-3-({[(5*R*)-5-isopropyl-3-(1-isoquinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxopentanoic acid in methyl t-butyl ether, adding a small amount of crystalline (3*S*)-5-fluoro-3-({[(5*R*)-5-isopropyl-3-(1-isoquinolinyl)-4,5-dihydro-5-isoxazolyl]carbonyl}amino)-4-oxopentanoic acid as a seed material to give a crystal, and recrystallizing this crystal from ethyl acetate/n-hexane solvent system.

12. (Currently Amended) A therapeutic composition ~~for preventing inflammation and apoptosis~~ comprising the caspase inhibitor compound of formula (1), salt, or

stereoisomer thereof as defined in claim 1 as an active ingredient together with the pharmaceutically acceptable carrier.

13. (Cancelled).

14. (Original) The composition according to claim 12 for the treatment of acute hepatitis or liver cirrhosis.

15. (Original) The composition according to claim 12 for the treatment of rheumatic arthritis.

16. (Original) The composition according to claim 12 which is formulated as an oral preparation, an injection, or a patch.

17. (Original) The composition according to claim 12 comprising the compound (Iii) as defined in claim 8 as an active ingredient.

18. (Original) The composition according to claim 12 comprising the compound (Iii-1) as defined in claim 10 as an active ingredient.

19. (Original) A process for preparing the therapeutic composition for preventing inflammation and apoptosis as defined in claim 12, comprising admixing the caspase inhibitor compound of formula (1), salt, or stereoisomer thereof as defined in claim 1 with pharmaceutically acceptable carrier.

20. (Currently Amended) A method for ~~preventing inflammation and~~ treating apoptosis, comprising administering an effective amount of the caspase inhibitor compound of formula (1), salt, or stereoisomer thereof as defined in claim 1 to a patient suffering from ~~inflammation and~~ apoptosis.

21. (Cancelled).

22. (New) The method according to claim 20, for the treatment of acute hepatitis or liver cirrhosis.

23. (New) The method according to claim 20, for the treatment of rheumatic arthritis.